

REMARKS

The Applicants wish to thank the Examiner for withdrawing the rejections and objections in the previous Office Action. Claims 1-6 are pending in the application. No new amendments are being introduced in this reply. Claims 1 and 4-6 have been newly rejected under § 102(b) as being anticipated by Heifetz et al (WO 00/68374) and claims 1-6 have been newly rejected under § 103 as being unpatentable over Heifetz alone or in view of Lundstrom (cited on Form PTO-892 filed 09/07/05).

Priority

According to the Examiner, the Applicants have not filed a certified copy of their foreign priority document (EPO 00126113.0) as required under 35 U.S.C. 119(b) and therefore cannot rely on the priority papers to overcome the rejections based on Heifetz (published on November 16, 2000).

In response, the Applicants' respectfully note that a certified copy of EPO 00126113.0 was filed June 21, 2002. For the Examiner's convenience, the Applicants are enclosing another copy of all the papers filed on June 21, 2002 (including the certified copy of EPO 00126113.0, the transmittal cover sheet, and the post card stamped by the Patent Office showing that the Patent Office received the certified copy of EPO 00126113.0 on June 26, 2002).

Claim Rejections Under 35 USC § 102

Claims 1 and 4-6 are rejected under § 102(b) as being anticipated by Heifetz et al. (WO 00/68374). The Examiner asserts that Heifetz teaches a process for inhibiting expression of a gene in a plant cell by the administration of a single-stranded sense fragment and a single stranded antisense RNA fragment capable of forming double-

stranded RNA (citing page 7) and that Heifetz teaches viral vectors for the introduction of said RNA fragments into plant cells (citing page 11).

First, the Applicants' respectfully note that Heifetz is not prior art under § 102(b) because it published on November 16, 2000 and the Applicants priority date for the invention is November 29, 2000 (EPO 00126113.0). As noted above, a certified copy of EPO 00126113.0 was in fact filed on June 21, 2002 as evidenced by the post card stamped by the Patent Office showing that the Patent Office received the certified copy of EPO 00126113.0 on June 26, 2002.

Second, to the extent that the rejection applies under section 102(a) or 102(e), the Applicants' respectfully note that Heifetz does not disclose or suggest the step of administering to cells or tissue both (a) a first set of viral particles consisting essentially of single stranded ribonucleic acid (ss RNA) which expresses a sense RNA strand (not antisense), and (b) a second set of viral particles consisting essentially of ss RNA which expresses an anti-sense RNA strand (not sense).

Although the Examiner states that page 11 of Heifetz teaches "viral vectors" for the introduction of RNA fragments into plant cells, it is clear that in fact Heifetz does not teach or suggest the use viral particles for the introduction of RNA fragments into plant cells - and certainly not two separate sets of viral particles one expressing sense and the other set expressing antisense as noted above.

In contrast to viral delivery, Heifetz only discloses the use of particle bombardment, PEG-mediated transformation, electroporation, and microinjection (not the use of viral particles) to introduce viral RNA fragments into cells. See page 10, lines 8-11 of Heifetz which states:

The RNA fragments are introduced in the cells by different transformation methods such as particle bombardment or PEG-mediated transformation or

electroporation. In another preferred embodiment . . . microinjection of the RNA fragments, are used.

The area on page 11 of Heifetz which the Examiner cites states only the following:

DNA molecules of the present invention are transformed into cells using methods well-known in the art or described below. The present invention also provides a DNA construct comprising DNA sequences of the present invention, a recombinant vector comprising such DNA constructs and a composition comprising DNA constructs of the present invention. In the present invention, the complementary region between the sense and antisense RNA fragments is desirably at least 15 nucleotides in length . . . (emphasis added)

A vector is defined as "the DNA of an agent (virus or plasmid) used to transmit genetic material to a cell or organism." Molecular Biology of The Cell, 4th edition (2002), p. G:36 of the Glossary. A vector is not the viral particle itself (a virion or virus). Heifetz does not disclose the use of viral particles as a method of introducing RNA fragments into plant cells.

No where does Heifetz disclose or suggest the actual use of viral particles themselves as a transformation method to introduce RNA fragments into plant cells (and it certainly does not disclose or suggest the use of two separate sets of viral particles one expressing sense and the other antisense as noted above). The invention of Heifetz relates to plant cells that are resistant to viral infection by introducing viral RNA fragments or viral DNA sequences into the cells through particle bombardment, PEG-mediated transformation, electroporation, and microinjection (not by the use of viral particles, let alone two separate sets of viral particles).

Again, in no instance does Heifetz teach or suggest infecting the same group of cells with two sets of viral particles: a first set of viral particles with RNA expressing the sense RNA strand (not anti-sense), and a second set of viral particles with RNA expressing the anti-sense RNA strand (not sense).

Accordingly, because Heifetz fails to disclose all the elements or steps of the claimed invention, the rejection under 35 U.S.C. § 102 should be withdrawn. (In order for a reference to anticipate a claim under 35 U.S.C. § 102, the reference must disclose every element or step of the claim. MPEP § 2131).

Claim Rejections Under 35 USC § 103

Claims 1 and 3-6 are rejected under 35 U.S.C. § 103 as being unpatentable over Heifetz in view of Lundstrom. Claims 1-2 and 4-6 are also rejected under 35 U.S.C. § 103 as being unpatentable over Heifetz alone. The Examiner asserts that although Heifetz does not teach the infection of cells with equal amounts of viral particles consisting of sense and antisense strands, it would have been obvious to one of ordinary skill in the art at the time the invention was made to infect cells with equal volumes of viral particles for the purposes of forming a dsRNA molecule. The Examiner also states that it would have been obvious to use an alphavirus vector, as taught by Lundstrom, to deliver RNA to plant cells, as taught by Heifetz.

The Applicants again note that (as stated above), Heifetz is not prior art under § 102(b)/103 because it published on November 16, 2000 and the Applicants priority date for the invention is November 29, 2000 (EPO 00126113.0). In addition, the following is respectfully submitted:

A. No Prima Facie Case of Obviousness Has Been Established

A *prima facie* case of obviousness has not been established because Heifetz (taken alone or in combination with Lundstrom) does not teach or suggest all the claim limitations. Under MPEP § 2143.03 in order to establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. If the prior art references do not disclose or suggest all of

the claim limitations either by themselves or in combination with each other, there can be no *prima facie* case of obviousness.

Here, the deficiencies in Heifetz are not cured by the addition of Lundstrom. Neither Heifetz nor Lundstrom teach or suggest the step of administering to cells or tissue **both** (a) a first set of viral particles consisting essentially of single stranded ribonucleic acid (ss RNA) which expresses a sense RNA strand (not antisense), and (b) a second set of viral particles consisting essentially of ss RNA which expresses an anti-sense RNA strand (not sense).

As stated above, Heifetz does not teach or suggest the use viral particles for the introduction of RNA fragments into plant cells - and moreover certainly not two separate sets of viral particles one expressing sense and the other antisense as noted above. In contrast to viral delivery, Heifetz only discloses the use of particle bombardment, PEG-mediated transformation, electroporation, and microinjection (not the use of viral particles) to introduce viral RNA fragments into cells. See page 10, lines 8-11 of Heifetz which states:

The RNA fragments are introduced in the cells by different transformation methods such as particle bombardment or PEG-mediated transformation or electroporation. In another preferred embodiment . . . microinjection of the RNA fragments, are used.

The area on page 11 of Heifetz which the Examiner cites states only the following:

DNA molecules of the present invention are transformed into cells using methods well-known in the art or described below. The present invention also provides a DNA construct comprising DNA sequences of the present invention, a recombinant vector comprising such DNA constructs and a composition comprising DNA constructs of the present invention. In the present invention, the complementary region between the sense and antisense RNA fragments is desirably at least 15 nucleotides in length . . .

Again, a vector is “the DNA of an agent (virus or plasmid) used to transmit genetic material to a cell or organism.” Molecular Biology of The Cell, 4th edition (2002), p. G:36 of the Glossary. A vector is not the viral particle itself (a virion or virus). Heifetz does not disclose the use of viral particles as a method of introducing RNA fragments into plant cells.

No where does Heifetz disclose or suggest the actual use of viral particles as a transformation method to introduce RNA fragments into plant cells (and it certainly does not disclose or suggest the use of two separate sets of viral particles one expressing sense and the other antisense as noted above). The invention of Heifetz relates to plant cells that are resistant to viral infection by introducing viral RNA fragments or viral DNA sequences into the cells through particle bombardment, PEG-mediated transformation, electroporation, and microinjection (not by the use of viral particles, let alone two separate sets of viral particles).

In no instance does Heifetz or Lundstrom teach or suggest infecting the same group of cells with two sets of viral particles: a first set of viral particles with RNA expressing the sense RNA strand (not anti-sense), and a second set of viral particles with RNA expressing the anti-sense RNA strand (not sense). Accordingly, there is no teaching in Heifetz or Lundstrom that discloses the use of two separate viral particle populations (wherein one population provides the sense strand instead of the anti-sense strand and the other population provides the anti-sense strand instead of the sense strand).

Thus, Heifetz (taken alone or in combination with Lundstrom) does not teach or suggest all the claim limitations for each claim of the present invention. Accordingly, it is respectfully submitted that a *prima facie* case of obviousness has not been established for this reason alone. Under MPEP § 2143.03 in order to establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. If the prior art references do not disclose or suggest all of

the claim limitations either by themselves or in combination with each other, there can be no *prima facie* case of obviousness.

B. There Are Surprising And Unexpected Results

In addition to arguments above, the Examples of the present application surprisingly demonstrate that when the sense and anti-sense fragments are provided by different vectors there is an inhibition of the expression of chromosomal cyclin genes. In contrast, when both sense and anti-sense fragments are provided in the same construct in the same vector inhibition of the expression of chromosomal cyclin genes does not occur (see Examples 6 & 7 on page 15 of the specification). Under MPEP § 2144-45, evidence of such surprising and unexpected results rebuts a *prima facie* case of obviousness.

All of the claims of the present invention require that cells or tissue be infected by two different sets of viral particles: one set providing the sense RNA and the other providing the anti-sense RNA. As shown in Example 7 (page 15 of the specification), when both sense and anti-sense sequences are cloned into the same construct in the same vector, there was no inhibition of the target gene(s) after infection. In contrast, as shown in Example 6, when the sense and anti-sense sequences are cloned separately into separate vector populations, there was inhibition of the target gene(s) after infection (which was even more potent than inhibition of cell growth by antibiotics [neomycin and zeocin], see page 15 of the specification). This represents surprising and unexpected results. Accordingly, it is respectfully submitted that these surprising and unexpected would rebut any assertion that the claimed invention is obvious (even if a *prima facie* case of obviousness had been established- which it has not for the reasons stated previously).

For all of the above reasons, the Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

Conclusion

Entry of the foregoing remarks is respectfully requested. No fee is believed to be due in connection with the filing of this Reply (other than for the RCE). However, if any other fee is deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,



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